



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Berglund et al.

Serial No.: 10/594,225

Filed: October 5, 2007

For: ANTI-ADHESIVE COMPOUNDS TO
PREVENT AND TREAT BACTERIAL
INFECTIONS

Examiner: S. Goon

Group Art Unit: 1623

Attorney Docket No.: 2676-7992US

CERTIFICATE OF MAILING

I hereby certify that this correspondence along with any attachments referred to or identified as being attached or enclosed is being deposited with the United States Postal Service as First Class Mail on the date of deposit shown below with sufficient postage and in an envelope addressed to the Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date

Signature

Name (Type/Print)

DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. JULIE BOUCKAERT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dr. Julie Bouckaert hereby declares:

1. I am a named inventor on the above-referenced patent application.
2. I am a post-doctoral fellow at the Virje Universiteit Brussel and an expert in the biology of molecular binding to the pilus of gram-negative bacteria. A copy of my curriculum vitae is attached.
3. I understand that in the Office Action mailed August 18, 2008, the Examiner has rejected claims 10-14 as assertedly being assertedly being obvious over Nagahori *et al.* (Chem. BioChem. (2002) vol. 3, p. 836-844) (hereinafter "Nagahori") in view of Choudhury *et al.* (Science, vol. 285, P. 1061-1066) (hereinafter "Choudhury") and Bouckaert (Glycoconjugate J., vol. 18, p. 31) (hereinafter "Bouckaert") (collectively hereinafter "the references").

4. Herein, I present the data originally present in Table 1 of the Specification of the above referenced application and provide the standard deviations of the K_d values in the column labeled SD K_d .

<i>Ligand</i>	<i>K_d SPR (nM)</i>	<i>SD K_d (nM)</i>	<i>ΔG° SPR (kcal/mol)</i>	<i>K_d Displace (nM)</i>	<i>ΔG° Displace (kcal/mol)</i>
mannose	2.3 10 ³	220	-7.6	4.1 10 ³	-7.3
methylαman	2.2 10 ³	115	-7.7	2.4 10 ³	-7.6
ethylαman	1.2 10 ³	235	-8.1	730	-8.3
propylαman	300	14.3	-8.9	400	-8.7
butylαman	151	16.8	-9.3	150	-9.3
pentylαman	25	1.6	-10.4	200	-9.1
hexylαman	10	2.9	-10.9	100	-9.5
heptylαman	5	1.6	-11.3	32	-10.2
octylαman	6.4	0.3	-11.2	28	-10.3
pNPαMan	86	58	-10.0	26	-10.3
MeUmbαMan	44	38	-10.5	12	-10.8

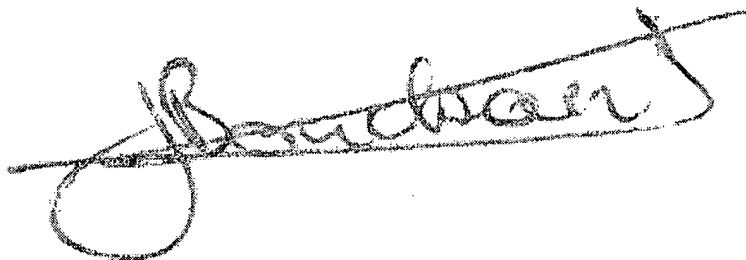
5. The data presented herewith indicate that one of ordinary skill in the art would find that the changes in the K_d value for the D-alpha-mannose with an n-pentyl group relative to unmodified mannose or D-alpha-mannose with an n-methyl or n-ethyl group to be statistically significant.

6. The experimental data presented herewith further indicate that one of ordinary skill in the art would find a two order of magnitude decrease in the K_d of D-alpha-mannose with an n-pentyl group relative to unmodified mannose or D-alpha-mannose with an n-methyl or n-ethyl group to be unexpected.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: __18-11-2008__ 18 November 2008

A handwritten signature in dark ink, appearing to read 'Bouckaert', with a large, stylized initial 'B' and a long horizontal stroke extending to the right.

— Dr. Julie Bouckaert —

CURRICULUM VITAE

Julie Maria Jozefa Bouckaert, Belgian, female, Ph.D.

Personal

- Born in Roeselare, Belgium, June 2, 1967, 41 y
 - Geevaertweg 18, 1640 Sint-Genesius-Rode, Belgium
 - tel 3226291988 fax 32 2 629.19.63 email bouckaej@vub.ac.be
 - <http://structuralbiology.be/Julie%20Bouckaert>
 - Married on September 5, 2001, to Savvas Nicos Savvides (born 13/08/1972 in Lefkosia, Cyprus)
 - 3 children: Imoh 11 y, Niels 6 y and Emilie 5 y
-

Professional

- Apr 1, 2008 – March 31, 2011: **Project Leader** in Bacterial adhesion
VIB Department of Molecular and Cellular Interactions, Belgium
Teacher in "Structure and Function of Proteins", VUB,
Structural Biology Brussels (<http://structuralbiology.be/>), Belgium
- Oct 1, 2004 – March 31, 2008: **Post-doctoral Fellow** (3rd mandate, FWO) & **Project Leader** VIB
Laboratory for Ultrastructure, VUB, Belgium
- Aug 1, 2002 – Sept 30, 2004: **Post-doctoral Fellow** (2nd mandate, FWO) & **Project Leader** VIB
Laboratory for Ultrastructure, VUB, Belgium
- Aug 15, 2000 – Jul 31, 2002: **Visiting Research Fellow** (Mobility grant, FWO)
Washington University School of Medicine, St. Louis, USA
Principal Investigator: Prof. Dr. Scott J. Hultgren.
- Oct 1, 1996 - Aug 15, 2000: **Post-doctoral fellow** (1st mandate, FWO)
Laboratory for Ultrastructure, Vrije Universiteit Brussel, Belgium
Principal Investigator: Prof. Dr. Lode Wyns

VUB= Vrije Universiteit Brussel (<http://www.vub.ac.be/>) - FWO= Fund for Scientific Research-Flanders
(<http://sun.fwo.be/>) - VIB= Flanders Interuniversity Institute for Biotechnology (<http://www.vib.be>)

Education

- Feb 1996: Doctor in the Applied Biological Sciences
Title of the thesis: "Mapping the structural features of metal- and carbohydrate binding of concanavalin A", Greatest Distinction
- Oct 1994 – Feb 1996: Doctorandus-assistent at the VUB
- Oct 1990 – Sep 1994: Doctorandus on 4 yearly grants of the IWONL (now IWT)
- Oct 1987 – Jun 1990: Engineer in Chemistry and Agricultural Sciences, at the VUB
1988 Distinction, 1989 Distinction, 1990 Great Distinction
- Oct 1985 – Jun 1987: Candidate Biology, RUCA, 1986 Great Distinction, 1987 Distinction
- Sep 1979 – Jun 1985: Primary and Secondary Education, Latin-Sciences, Royal Atheneum, Mortsel
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Principal Scientific Activities and Responsibilities

Work at the bench has always been my passion and major activity. I still like to follow the rapid changes in the multiple scientific environments involved in my research and work closely together with the students. I have been in the USA for 2 years (2000-2002) to initiate our current research on bacterial adhesins. I have

Curriculum vitae - Julie Bouckaert - 21-08-2008

travelled for meetings, workshops and collaborations selectively, to guarantee high-quality output and balance with family life. I have co-organized 3 national and 1 international meetings, 1 workshop, tutored 13 students during their dissertations (1997-today) and 4 PhD students (2002- today). I have given practicals in Crystallography and in Physicochemistry of Macromolecules since I was a PhD student and will teach a course on the Structure and Function of Proteins. Currently Prof. Henri De Greve and myself run the Bacterial Adhesion project with 3 doctorandi and 1 technician.

My most recent contributions to the field of glycobiology

Glycobiology summer school, Brussels, Belgium, 4-6 June 2008: **Organiser, Speaker and Chair**
XVIIIth Joint Meeting, Lesquin-Lille, France, 4-6 Nov 2007 **Speaker and Chair of the session Traffic**
Eurocarb14, Luebeck, Germany, 4-7 Sep 2007 **Speaker**

Publications

10 most significant research publications, with S.C.I. impactfactor of the publication year and number of cites

Bouckaert, J., Loris, R., Poortmans, F., and Wyns, L. (1995). Crystallographic structure of metal-free concanavalin A at 2.5 angstrom resolution. *Proteins Struct. Funct. Genet.* 23: 510-524. IF 3.739, cites 35

Loris R., Hamelryck T., Bouckaert J., Wyns L (1998). Legume lectin structure. *Biochim Biophys Acta* 1383 (1): 9-36. Review. IF 2.478 cites 199

Bouckaert, J., Hamelryck, T., Wyns, L. & Loris, R. (1999). Novel structures of plant lectins and their complexes with carbohydrates. Review. *Curr. Opin. Struct. Biol.* 9: 572-577. IF 8.633, cites 48

Hung, C.S.[@], Bouckaert, J.[@], Hung, D., Pinker, J., Winberg, C., DeFusco, A., Auguste, C.G., Strouse, R., Langermann, S., Waksman, G., & Hultgren S. (2002). Structural basis of tropism of *Escherichia coli* to the bladder during urinary tract infection. *Mol. Microbiol.* 44, 903-915. [@]co-1st authors IF 5.832, cites 79

Buts, L.[@], Bouckaert, J.[@], De Genst, E., Loris, R., Oscarson, S., Lahmann, M., Messens, J., Brosens, E., Wyns, L., De Greve, H. (2003) The fimbrial adhesin F17-G of enterotoxigenic *Escherichia coli* has an immunoglobulin-like lectin domain that binds *N*-acetylglucosamine. [@]co- 1st authors *Mol. Microbiol.* 49(3):705-715. IF 5.563, cites 19

Bouckaert, J., Berglund, J., Schembri, M., De Genst, E., Cools, L., Wuhrer, M., Hung, C.-S., Pinkner, J., Slättegård, R., Zavialov, A., Choudhury, D., Langermann, S., Hultgren, S. J., Wyns, L., Klemm, P., Oscarson, S., Knight, S. D. & De Greve, H. (2005). Receptor binding studies disclose a novel class of high-affinity inhibitors of the *Escherichia coli* FimH adhesin. *Mol. Microbiol.* 55: 441-455. IF 6.203, cites 39

Bouckaert J., Mackenzie J., de Paz J.L., Chipwaza B., Choudhury D., Zavialov A., Mannerstedt K., Anderson J., Piérard D., Wyns L., Seeberger P.H., Oscarson S., De Greve H. & Knight S.D. (2006). The affinity of the FimH fimbrial adhesin is receptor-driven and quasi-independent of *Escherichia coli* pathotypes. *Mol. Microbiol.* 61: 1556-1568. IF 5.634, cites 7

Touaibia M, Wellens A, Shiao TC, Wang Q, Sirois S, Bouckaert J & Roy R. (2007). Mannosylated G(0) dendrimers with nanomolar affinities to *Escherichia coli* FimH. *ChemMedChem* 2: 1190-1201. IF 2.825, cites 6

De Greve, H., Wyns, L., and Bouckaert, J. (2007). Combining sites of bacterial fimbriae. *Curr. Opin. Struct. Biol.* 17: 412-418. IF 10.150, cites 1

Wellens A, Garofalo C, Nguyen H, Van Gerven N, Slättegård R, Hernalsteens JP, Wyns L, Oscarson S, De Greve H, Hultgren SJ & Bouckaert J. (2008). Intervening with urinary tract infections using anti-adhesives based on the crystal structure of the FimH – oligomannose-3 complex. *PloS One* 3(4): e2040. cites 1

Press release

<http://www.vib.be/VIB/EN/News+and+press/Press+releases/VIB+-+Press+Releases+2004-2005.htm#urineeng>
Progress toward a new remedy for chronic urinary tract infections? Publication date Feb 10, 2005

Patents

International publication number and date: WO 2005/089733 A2, Sep 29, 2005
Anti-adhesive compounds to prevent and treat bacterial infections.

RCSB Protein data bank

52 protein crystal structures deposited (<http://www.rcsb.org/pdb/home/home.do>)